RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)									DATE February 1999	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 3							R-1 ITEM NOMENCLATURE Medical Advanced Technology Program PE 0603002D8Z			
COST*(In Millions)*	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to Complete	Total Cost
Total Program Element (PE) Cost	2.848	2.130	2.007	2.057	2.091	2.133	2.175	2.224	Continuing	Continuing
Risk Assessment and Biamedical Applications/P506	2.848	2.130	2.007	2.057	2.091	2.133	2.175	2.224	Continuing	Continuing

(U) A. Mission Description and Budget Item Justification

(U) BRIEF DESCRIPTION OF ELEMENT

(U) This program supports efforts in advanced technology development to provide biomedical strategies for preventing, treating, assessing and predicting casualties from ionizing radiation, either alone or in combination with biological warfare (BW)/chemical warfare (CW) agents. It is directed at the need for the Department of Defense (DoD) to be prepared to execute military missions within radiation environments, to manage radiation crises associated with terrorist activities, and for consequence management in the event of nuclear weapons detonation. The DoD is ethically committed to protection of Service members from the adverse health effects of ionizing radiation to the fullest extent consistent with operational requirements. The program incorporates findings from basic and applied research into highly integrated and focused advanced technology development studies to produce: (1) protective and therapeutic strategies, (2) tools to measure radiation exposure to military personnel, and (3) accurate models to predict casualties, particularly in combined nuclear-biological-chemical (NBC) environments. This program is executed by the Armed Forces Radiobiology Research Institute (AFRRI) which, due to its multidisciplinary staff and exceptional laboratory and radiation facilities, is uniquely qualified to carry out this mission. Because national laboratories operated by the Department of Energy no longer support advanced research relevant to military medical radiobiology, AFRRI is currently the sole laboratory in existence with the combined capabilities needed to conduct this research.

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(U) Project Number and Title: P506 Risk Assessment and Biomedical Applications

(U) PROGRAM ACCOMPLISHMENTS AND PLANS

(U) FY1998 Accomplishments:

(U) Completed a pilot demonstration of an improved clinical support protocol for acute, potentially fatal radiation injury. Continued assessment and optimization of a combined (prophylaxis/therapeutic) treatment modality for enhancing survival following acute, lethal irradiation. ($ 0.718 Million)

(U) Demonstrated the feasibility of using implanted capsules to provide sustained and effective delivery of radioprotective drugs. Improved efficacy of implanted 'slow-release' drug capsules by instituting use of therapeutic drug assays for monitoring blood levels of radioprotective drugs during protocol optimization studies. ($ 0.402 Million)

(U) Developed simplified sample preparation procedure used with chromosome aberration assays for radiation dose assessment. The procedure will facilitate fielding of chromosomal aberration assays to advanced medical treatment facilities. Completed initial studies extending the application of radiation dose measuring protocols to incremental doses of gamma and fission neutrons. ($ 0.524 Million)

(U) Developed protocols to enable measurement molecular markers (oncogene expression, mitochondria DNA deletions) by means of a compact, portable field-deployable platform. This effort exploits a dual-use potential for a delivery platform under development elsewhere for military use that can rapidly measure nucleic acid changes by the polymerase chain reaction (PCR). ($ 0.619 Million)

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(U) Established the capability to integrate the health con sequences of radiation/ BW agent interactions into the Consequence Assessment Tool Set (CATS). Initiated computer-modeling efforts to incorporate combined injury data into CATS. ($ 0.293 Million)

(U) Continued development of simple method to measure uranium i n urine of military personnel to provide a rapid, field-based clinical assay for depleted uranium (DU) exposure, and submitted the procedure for patent application. ($ 0.292 Million)

(U) FY1999 Plans:

(U) Assess efficacy of a modified, nontoxic radioprotective dru g combination together with an improved clinical regimen for maximizing the prevention of acute and potentially fatal radiation injury. ($ 0.168 Million)

(U) Initiate development of preventive treatments for the long -term health consequences associated with radiation exposure. Design and assess implanted, slow-release drug capsules. ($ 0.169 Million)

(U) Initiate combined treatment protocol studies aimed at combating radiation-associated nausea and tissue injury following acute exposures. ($ 0.168 Million)

(U) Complete development of initial *in vitro* radiation calibration curves for a simplified chromosome aberration measurement procedure. Further optimize sample preparation protocols for automated analysis in deployed medical treatment facilities. Develop automated cytological platforms for rapid analysis of blood samples from mass casualties. ($ 0.369 Million)

(U) Develop software tools to manage biodosimetric data for field use and provide an integrated system for measurement of radiation exposures. Test rapid, forward-fieldable screening assays for estimating radiation exposure. Validate newly developed biodosimetry methods under collaborative agreements and human-use protocols at clinical radiotherapy centers for testing radiation therapy patients. ($ 0.504 Million)

(U) Develop initial computer program for CATS to predict casualty rates in operational forces using experimental data from animal studies that reveal enhanced mortality from combined exposures to radiation and bacteria. The program will have the capability to superimpose and analyze the two footprints in a single output. ($ 0.321 Million)

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(U) Provide recommendations to physicians for treatment of exposure to DU based on continuing studies of DU toxicity and tissue distribution. Continue development of simple method to measure uranium in urine of military personnel. ($ 0.431 Million)

(U) FY2000 Plans:

(U) Assess safety and efficacy of implanted, slow-release, radioprotective treatment devices. Perform standard toxicology assessments on treatments relative to specific blood or tissue levels of radioprotectants. ($ 0.476 Million)

(U) Continue *in vivo* studies validating chromosome aberration assay over a broad dose range and partial-body exposure situation. Test improved cytological analysis platforms using simple and easy to perform sample protocols. ($ 0.347 Million)

(U) Complete initial-phase optimization of PCR-based assays for measuring multiple molecular biomarkers using field deployable platform. Continue studies to validate screening assays for measuring radiation exposure. ($ 0.474 Million)

(U) Provide recommendations for addressing any changes in efficacy of *B. anthracis* vaccine upon exposure to ionizing radiation. Initiate efforts to incorporate performance-degrading consequences from combined radiation/bacterial and radiation/pyridostigmine exposures into casualty prediction models. ($ 0.303 Million)

(U) Complete development of method to measure uranium in urine of military personnel; provide protocol to application centers for assessment as a fieldable methodology. ($ 0.407 Million)

(U) FY2001 Plans:

(U) Design and test easy-to-use autoinjector devices for delivery and implantation of the slow-release drug capsules for treatment of injuries associated with radiation exposure. ($ 0.487 Million)

(U) Further validate biological marker assays for radiation exposure by determining their performance characteristics in measuring (1) exposure to gamma rays at low-dose rates and (2) prior radiation exposures. The availability of a prior-exposure assessment capability is essential to permit dose assessment when analysis is delayed or when exposures are protracted. ($ 0.356 Million)

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(U) Conducted validation analysis of the automated imaging platform for radiation dose assessment. Continue to develop and validate multiple molecular biomarker approach for diagnostic biodosimetric applications. ($ 0.486 Million)

(U) Provide computer module for Consequence Assessment Tool Set (CATS) to predict mortality from interactions of radiation and *B. anthracis*. Initiate efforts to incorporate interactions of radiation with viral agents into casualty prediction models. ($ 0.310 Million)

(U) Provide recommendations to physicians for treatment of exposure to Depleted Uranium (DU) based on findings from AFRRI immunotoxicity and neurotoxicity studies. ($ 0.418 Million)

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(U) B. Program Change Summary	FY1998	FY1999	FY2000	FY2001	Total Cost
Previous Presidents Budget	2.672	2.136	2.041	2.094	Continuing
Appropriated Value	2.778	2.136	0	0	Continuing
Adjustments to Appropriated Value					
a. Congressionally Directed Undistributed Reduction	-0.106	-0.006	0	0	
b. Rescission/Below-threshold Reprogramming, Inflation Adjustment	0	0	-0.034	-0.037	
c. Other	0	0			
Current Presidents Budget	2.848	2.130	2.007	2.057	Continuing

Change Summary Explanation: Funding changes are due to congressional undistributed reductions and inflation adjustments.

(U) Funding: Changes are due to congressional undistributed reductions and inflation adjustments.

(U) Schedule: N/A

(U) Technical: Changes are due to congressional undistributed reductions and inflation adjustments.

(U) C. OTHER PROGRAM FUNDING SUMMARY COST: N/A

(U) D. ACQUISITION STRATEGY: N/A

(U) E. SCHEDULE PROFILE: N/A